ラット摘出還流肺を用いた物質吸収に関する研究Ⅳ
～蛍光標識ポリアスパルタマイド誘導体の吸収機構について～

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Solute Absorption from the Airways of the Isolated Rat Lung. Ⅳ. Mechanisms of Absorption of Fluorophore-Labeled Poly-α, β-[N(2-Hydroxyethyl)-DL-Aspartamide]

The pulmonary absorption kinetics of a single molecular weight distribution (MWD) of fluorophore-labeled poly-α, β-[N(2-hydroxyethyl)-DL-aspartamide] (F-PHEA), a hydrophilic and biocompatible synthetic polypeptide, were studied} in the isolated, perfused rat lung (iprl) as functions of administered polymer concentration, dose, vehicle, and presence and absence of fluorophore. The MWD was characterized before and after absorption by measurement of weight- and number-averaged molecular weights (Mw and Mn, respectively) using high-performance gel-permeation chromatography. Values for Mw and Mn were 8.6 and 5.3 kD before,and 6.7 and 4.7 kD after, absorption into the Perfu, sate; there was no significant metabolism and the MWD of the absorbed polymer was independent of both dose and sampling time over a 3-hr period. F-PHEA failed to show any evidence of aggregation in solution or changes in dose distribution within the airways as functions of increasing polymer concentration and dose. A concentration ranging study indicated the presence of a saturable, carrier-mediated transport process for F-PHEA with a maximum absorption rate, Vmax, of approximately 180 μg or 0.027 μmol/hr. Coadministration of fluorophore-free PHEA was capable of depressing the absorption of F-PHEA. The transport process for F-PHEA appeared to have a molecular weight limit of about 7 kD for this hydrophilic polymer.

分子量分布の狭いポリマー(F-PHEA)を蛍光標識し、標識体(F-PHEA)の肺呼吸

について検討した。ラット摘出還流肺の気管よりF-PHEAを投与し、還流液中に出現したものの分子量分布を調べたところ投与液中に比べ低分子側にシフトした。F-PHEAは肺でほとんど代謝されず、このような分子量分布の変化は投与量やサンプリングタイムに影響されなかった。また、F-PHEAの肺呼吸には飽和がみられ、そのVmaxは0.027 μmol/hrであった。非標識体を同時投与すると標識体の吸収は抑制された。

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